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Christine Todd Whitman, Administrator
US Environmental Protection Agency
Ariel Rios Building
Room 3000, #1101-A
1200 Pennsylvania Avenue, NW
Washington, DC 20460

Subject: Comments on the HPV test plan for 2-chloropyridine

Dear Administrator Whitman,

The following are comments on the test plan for 2-chloropyridine (CAS RN 109-09-1) for the HPV program, submitted by Arch Chemicals, Inc. (Arch). These comments are submitted on behalf of the Physicians Committee for Responsible Medicine, People for the Ethical Treatment of Animals, the Humane Society of the United States, the Doris Day Animal League, and Earth Island Institute. These animal, health and environmental protection organizations have a combined membership of more than ten million Americans. We appreciate the assistance of Dr. Richard Thornhill of the PETA Research and Education Foundation in preparing these comments.

Arch proposes conducting a mammalian repeat-dose toxicity test (OECD no. 407) and a combined reproductive and developmental toxicity test (OECD no. 421) on 2-chloropyridine, apparently due to lack of sufficient data. These tests will kill at least 715-740 mammals. Our criticisms of Arch's test plan are as follows.

First, we do not understand why Arch proposes conducting separate repeat-dose and reproductive/developmental tests, when the combined repeat-dose, reproductive and developmental test (OECD no. 422) would address both SIDS endpoints and reduce the number of animals killed versus the two tests separately. Please refer to both the October 1999 agreement to reduce the number of animals killed in the HPV program and the Dec. 2000 Federal Register notice encouraging participants to use the combined test.

Second, we must point out that repeat-dose studies of 2-chloropyridine have been carried out previously. These studies were carried out under the National Toxicology Program, and involved topical administration for 14 and 90 days (NIH 2002, p. 24). We have been unable to find any information about the results of these studies, but they could be obtained by contacting the National Institutes of Health, and Arch should do so, in order to take all available data into account before proposing experiments on animals.

Third, Arch provides insufficient information about the human exposure to 2-chloropyridine and the industrial processes in which it is used. From the description given in the test plan (p. 3), it is possible that 2-chloropyridine is a closed-system intermediate. This possibility is also suggested by the fact that the National Institute for Occupational Safety and Health's National Occupational Exposure Survey did not cover this compound (http://www.cdc.gov/noes/noes1/noescas1.html). If 2-chloropyridine is a closed-system intermediate, repeat-dose and reproductive data are not required, as stated by the EPA:

> "Participants shall not develop sub-chronic or reproductive toxicity data for the HPV chemicals that are solely closed system intermediates" (Wayland 1999).

Although the developmental toxicity endpoint might still be needed, developmental data can now be obtained using an *in vitro* test; the rodent embryonic stem cell test, which is appropriate for a screening level program such as the HPV program. This test has recently become commercially available in the US, and last year it was validated by the European Centre for the Validation of Alternative Methods, after which the Centre's Scientific Advisory Committee concluded that it was ready to be considered for regulatory purposes (Genschow 2002). We hope that Arch will feel free to contact us for advice about the laboratory that is currently conducting this test.

To conclude, Arch should make a more thorough search for relevant available data, and should re-examine carefully whether the proposed tests are necessary under the terms set by the EPA.

Thank you for your attention to these comments. I look forward to a prompt and favorable response to our concerns. I can be reached at 202-686-2210 ext. 302 or via email at Csandusky@pcrm.org.

Sincerely,

Chad B. Sandusky, PhD
Director of Research

Kristie Stoick, MPH
Research Analyst

References

Genschow, E., *et al.*, "The ECVAM international validation study on *in vitro* embryotoxicity tests: Results of the definitive phase and evaluation of prediction models", *Alternatives to Laboratory Animals* 30: 151-76, 2002.

National Institutes of Health, *The National Toxicology Program: Annual Plan for Fiscal Year 2001*, NIH publication no. 02-5092, January 2002, http://ntp-server.niehs.nih.gov/htdocs/2001ap/ap2001.pdf.

Wayland, S.H., *Letters to manufacturers/importers*, October 14, 1999, http://www.epa.gov/chemrtk/ceoltr2.htm.